REMARKS

The Applicants have carefully considered the Office Action mailed June 1, 2007 and have the following comments.

Applicants thank the Examiner for indicating that the previous objection to the claims has been withdrawn.

Rejections Pursuant to 35 U.S.C. 112(2)

Claims 41-42 were rejected as lacking clarity. Both of these claims have now been amended to eliminate the word "either". The resulting claims, as so amended, are subitted to now be clear and unambiguous, and therefore Applicants respectfully ask that this rejection be withdrawn.

Rejections Pursuant to 35 U.S.C. 112(1)

Written Description

Claims 16-17, 32-38 and 40-46 were rejected as allegedly lacking adequate written description in the specification. Applicants respectfully again traverse this rejection, and hereby incorporate by reference the arguments made in the Amendment filed November 10, 2006. In addition, Applicants have the following comments.

Upon review of the June 1, 2007 Office Action, Applicants note that the Examiner now acknowledges that claim 16 recites the structure of the at least one module of the streptavidin binding peptide (see page 3, 2nd paragraph, line 6).

However, the Examiner continues to reject the indicated claims as allegedly lacking adequate

written description under 35 USC 112(1) , on the basis that the fusion protein of claim 16 allegedly does not set forth the required structure of the claimed fusion protein because the "protein moiety to which the streptavidin peptide is linked is not identified by, for example, amino acid sequence. See e.g., Office Action of June 1st 2007 at page 3, second paragraph, lines 1 to 3: "[t]he claims do not set forth the structure [of the protein], to make a correlation between structure and function."

Applicants respectfully but strenuously disagree with this statement, which is clearly central to the Examiner's rationale for rejecting these claims.

On pages 3 and 5 of the June 1st, 2007 Office Action the Examiner states "[a]dditionally, the claimed invention is drawn to a streptavidin mutein, a full-length protein, protein fragment, or protein mutant." On page 9 of the same Office Action the Examiner states that claim 16 comprises a streptavidin mutein. None of these statements is accurate. Claim 16 is drawn to a fusion protein comprising a streptavidin-binding protein linked to a protein, wherein the streptavidin-binding portion of the fusion protein comprises modules which each bind either streptavidin or a streptavidin mutein. Therefore while, as explained below, the "protein" moiety of the fusion protein may be any protein, none of the claims are drawn specifically to a streptavidin mutein.

In their reply to the last Office Action Applicants made amply clear that the precise identity (in terms of amino acid sequence) of the protein to which the streptavidin binding peptide is fused is not of importance (or, stated positively, is immaterial) to their invention. This is also evident to the person of ordinary skill in the art from the specification, which states, at page 8, at lines 18-24, "[a]n essential feature of the peptides of the invention is the fact that they are not 2 separate tags but are a sequential arrangement of at least 2 streptavidin-binding individual modules. In this way, the binding properties [i.e., the function] are determined by the streptavidin-binding ditag or multitag and are independent of the protein to be fused thereto." (Emphasis added.) Thus, the protein can be any protein of interest that is, for example, capable

of being recombinantly produced (see pages 1-3 of the present specification).

For this invention, all that is required of the linked protein is that it comprise amino acids linked by peptide bonds. This is conveyed by the Applicants' use of the term "protein". *See* WORLD OF BIOLOGY, 2005-2006 Thomson Gale: "[a] peptide is an organic molecule consisting of two or more amino acids linked through an amide linkage called a peptide bond . . . longer chains are called proteins."

There is absolutely no *per se* rule that a claim involving a protein must recite an amino acid sequence. In one of its recent decisions on this subject the Court of Appeals for the Federal Circuit stated "[t]he descriptive text needed to meet . . . [the written description requirement] varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science." *Capon v. Eschhar,* 76 USPQ2d 1078 (Fed. Cir. 2005) (emphasis added).

Thus, since the scope and nature of the present invention requires no particular characteristic of the linked protein portion of the claimed fusion protein (beyond the well-known definition of the term "protein"), the identification of this moiety of the claimed fusion protein as a "protein' is complete, precise, and perfectly sufficient to inform the person of ordinary skill in the art that the inventor was in possession of this part of the invention as claimed (e.g., in claim 16) at the time of filing. Furthermore the specification goes far beyond this in describing the invention. Thus, beginning at page 2, line 16 the specification indicates:

> A universal solution for these questions is in principle based on the slight modification of a recombinant gene during cloning with nucleotide sequences which code for "peptide tags". It is important in this connection that the peptide tag has suitable binding properties for a receptor. In practice, utilization of such a peptide tag is as follows:

> After or during expression, the target protein of interest is modified by a peptide tag. The known and well-characterized properties of the peptide tag for binding to its receptor in various assay methods are then available for further analysis of the target protein. Normally, the affinity tag is initially used for purifying the fusion protein by means of an immobilized receptor. It is important for purification by affinity chromatography that the recombinant fusion protein can again be eluted from the solid phase under mild conditions. After purification it may be desirable to be able to utilize the peptide tag for immobilizing the recombinant target protein to a solid phase such as the wall of a microtiter plate well, for example. Normally, a particularly tight binding is desired here, i.e. the fusion protein should not detach again from the solid phase under any circumstances during the assay method.

Thus, we submit that it is absolutely clear to the person skilled in the art that the nature of the protein of interest to which the streptavidin binding peptide is fused is not important at all, but at any protein of interest that can, for example, be recombinantly produced can be used. With full consideration of the nature of this invention, the specification fully describes the invention (including the required nexus between structure and function) in a manner that conveys to the person of ordinary skill in the art exactly what the inventors have invented.

Enablement

Claims 16-17, 32-34, 36-37, 40-45 and 47 were again rejected as drawn to an invention lacking enablement under 35 USC §103 in the specification. Although the *Wands* factors are not a mandatory framework of enablement analysis, Applicants set forth a detailed analysis of these factors in the November 13, 2006 Reply, and hereby incorporate by reference that analysis as part of this response. The Applicants again traverse this rejection.

In support of the understanding of the person skilled in the art at the time the present application was filed, Applicant has amongst other arguments already pointed to U.S. Patents

5,506,121 and 6,103,493. Both patents are issued before the filing date of the present application and disclose fusion proteins comprising any protein linked with a streptavidin binding peptide (an affinity peptide). Applicant would further like to call the Examiner's attention to US Patent 5,310,663 issued May 10, 1994 that is directed to fusion proteins of the hexa-histidine tag (His6-tag) that is discussed on page 3, lines 4-13 of the present specification. Claim 1 of US Patent 5,310,663 reads:

1. A DNA sequence coding for a fusion protein comprising a biologically active polypeptide or protein linked by its amino- or carboxy-terminus to one or two affinity peptides, which peptides have from 2 through 6 adjacent histidine residues.

As can be seen, claim 1 of the '663 patent uses the substantially same wording as present claim 16 in relation to the characterization of the polypeptide and the arrangement of the affinity peptide (here: the His6 tag) to the protein of interest.

Additionally, the '663 patent also clearly demonstrate that the art of protein purification, expression of fusion proteins, and affinity purification was considerably further advanced in 2001, when the priority application was filed, than the Examiner gives credit for. The Examiner's reliance on Wells, a reference from 1990, does not provide any information regarding the state of the art on the filing date of the present application. In particular, at the priority date it was well within the knowledge of one of ordinary skill in the art how to construct a nucleic acid expression vector (i.e., on the nucleic acid level) in which an affinity peptide such as the streptavidin-binding peptide of the present invention is fused C-terminally or N-terminally to a protein of interest, and thus produce the fusion protein in a suitable host cell expression system.

As further evidence of the knowledge of the person skilled in the art at the time of filing the present application, the Examiner's attention is called to Patent No. 5,654,176, issued August 5, 1997 and U.S. 5,292,646 issued March 8, 1994. These patents discloses fusion proteins of

glutathione-S-transferase (which acts as an affinity peptide) which contain any suitable protein for the purification of these proteins (see claim 1 of US 5,654, 176), and fusion of proteins of thioredoxin with a non-eucaryotic fusion partner (cf. claim 1 and claim 15 of Patent No. 5,292,646).

Thus, based on these above evidence, as well as the wealth of experimental data contained in the present application (as explained in Applicants' Reply of 10 November, 2006) we submit that the present claims are fully enabled by the disclosure of the present application.

Rejoinder

Because the present composition claims are now thought to be in condition for allowance, Applicants hereby respectfully ask the Examiner to rejoin and examine withdrawn method claims 19-26 in accordance with MPEP §821.04, since these method claims depend and incorporate all the limitations of claims 16, or 17.

CONCLUSION

For the reasons given above, the Applicants submit that the claims, as amended, are now in condition for allowance, and that method claims 19-26 should be rejoined and examined.

A two-month extension of time to reply is thought to be due in connection with this communication, as it is being filed within two months following the expiration of the three month shortened statutory period set in the Office Action. Applicants hereby authorize the Commissioner to use Deposit Account 50-4004 for the payment of this and any other fee that may be due in connection with this communication, or to credit any overpayment. If there are any questions associated with this communication, the Examiner is invited to telephone the undersigned at the telephone number listed.

Respectfully submitted,

Dated: 11/1/07

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